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# Research Publications Featuring the SH800 Cell Sorter for Genomics Applications

Recent advancements in single-cell genomics and multi-omics analysis have significantly increased our comprehension of cellular diversity and function. These studies offer a thorough exploration of cellular biology, unveiling insights into various aspects including cellular heterogeneity, tissue development, disease mechanisms, cellular communication, and therapeutic development.

The SH800 cell sorter has been instrumental in advancing these research efforts by providing researchers the capability to accurately isolate and sort specific cells or cellular components from complex samples. This capability is essential for acquiring the pure and viable cell populations necessary for generating dependable sequencing data in subsequent analyses. Additionally, the SH800's high throughput sorting rate enables efficient identification of rare cell populations. Furthermore, the system's versatility extends to sorting a wide variety of sample types based on different criteria such as surface markers or fluorescence intensity, making it an indispensable tool across diverse research applications spanning various biological systems.

The following table showcases the extensive application of Sony cell sorters in isolating viable cells as well as high-integrity nuclei from diverse sources for genomics analyses.

Research Area	Featured Publications	Experiment
Epigenomics /Multi-omics	Kuppe C, Ramirez Flores RO, Li Z, et al. Spatial multi-omic map of human myocardial infarction. <i>Nature</i> . 2022;608:766-777. <u>PubMed</u>	Heart tissue underwent dicing and homogenization, followed by addition of nuclei isolation buffer and RNase inhibitor. Mechanical dissociation with pestles was conducted, and the resulting nuclei were stained with DAPI and sorted using a Sony SH800 system to enhance concentration. The isolated nuclei suspensions were utilized for downstream RNA-seq and ATAC-seq analyses.
Developmental Biology	Zanini F, Che X, Knutsen C, et al. Developmental diversity and unique sensitivity to injury of lung endothelial subtypes during postnatal growth. <i>Iscience</i> . 2023;26:106097. PubMed	Using the SH800 system, lung endothelial cells were sorted into pre-filled 384-well plates containing lysis buffer, based on endothelial (CD31), epithelial (CD326), immune CD45 markers, and viability dye (SYTOX™ blue). Sorting was carried out using a 100-µm sorting chip in ultra-purity mode. Post-sorting, cells underwent transcriptional profiling using Smart-seq2 to generate libraries.
Cell Atlas	Rhodes CT, Thompson JJ, Mitra A, et al. An epigenome atlas of neural progenitors within the embryonic mouse forebrain. <i>Nat Commun</i> . 2022;13:4196. PubMed	Embryonic mouse tissue underwent protease treatment and gentle mechanical dissociation. Cells were stained with DRAQ5 and DAPI, filtered, and processed on an SH800 cell sorter to isolate live cells. The resulting cell suspensions were employed for scRNA-seq analysis utilizing the 10x Genomics platform.
Disease Progression	Wang G, Chiou J, Zeng C, et al. Integrating genetics with single-cell multiomic measurements across disease states identifies mechanisms of beta cell dysfunction in type 2 diabetes. <i>Nat Genet</i> . 2023;55:894-994. PubMed	Human pancreatic islets were chemically and mechanically homogenized, followed by centrifugation to obtain nuclei suspensions. The SH800 cell sorter was utilized to remove debris and enrich the nuclei sample. Sorted nuclei subsequently underwent downstream RNA-seq and ATAC-seq analyses.
Neurobiology	Kaya T, Mattugini N, Liu L, et al. CD8+ T cells induce interferon-responsive oligodendrocytes and microglia in white matter aging. <i>Nat Neurosci.</i> 2022;25:1446-1457. PubMed	Viable oligodendrocytes and astrocytes from corpus callosum and optical tracts were isolated utilizing the SH800 cell sorter. Single cells were dispensed into 96-well plates, and sequencing libraries were generated via Smartseq2 to determine cell-type composition.

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Research Area	Featured Publications	Experiment
Immunology	Huuhtanen J, Bhattacharya D, Lönnberg T, et al. Single-cell characterization of leukemic and non-leukemic immune repertoires in CD8+ T-cell large granular lymphocytic leukemia. <i>Nat Commun</i> . 2022;13:1981. PubMed	CD45+ cells from freshly thawed T-Cell Large Granular Lymphocytic Leukemia (T-LGLL) and healthy samples were isolated using the Sony SH800 cell sorter. Subsequently, single-cell RNA sequencing (scRNA-seq) and T-cell receptor alpha-beta (TCR $\alpha$ $\beta$ ) libraries were prepared utilizing the 10x Genomics platform.
Methods Development	De Rop FV, Hulselmans G, Flerin C, et al. Systematic benchmarking of single-cell ATAC- sequencing protocols. <i>Nat Biotechnol</i> . 2023. doi: 10.1038/s41587-023-01881-x. <u>PubMed</u>	Thawed PBMC samples were mechanically homogenized, and the SH800 system was employed to remove debris, quantify, and sort nuclei into two plates. Sorted nuclei were utilized for s3-ATAC sequencing and PCR amplification.

# **Selected Additional Publications**

## **Epigenomics**

Ishii S, Kakizuka T, Park S-J, et al. Genome-wide ATAC-see screening identifies TFDP1 as a modulator of global chromatin accessibility. *Nat Genet.* 2024. doi: 10.1038/s41588-024-0168-1. PubMed

Lareau CA, Liu V, Muus C, et al. Mitochondrial single-cell ATAC-seq for high-throughput multi-omic detection of mitochondrial genotypes and chromatin accessibility. *Nat Protoc.* 2023;18:1416-1440. PubMed

Spracklin G, Abdennur N, Imakaev M, et al. Diverse silent chromatin states modulate genome compartmentalization and loop extrusion barriers. *Nat Struct Mol Biol.* 2023;30:38-51. <u>PubMed</u>

Battaglia S, Dong K, Wu J, et al. Long-range phasing of dynamic, tissue-specific and allele-specific regulatory elements. Nat Genet. 2022;54:504-1513. <u>Nature</u>

Kuppe C, Ramirez Flores RO, Li Z, et al. Spatial multi-omic map of human myocardial infarction. *Nature*. 2022;608:766-777. PubMed

Fang R, Preissl S, Li Y, et al. Comprehensive analysis of single cell ATAC-seq data with SnapATAC. *Nat Commun.* 2021;12:a1337. Nature

Mulqueen RM, Pokholok D, O'Connell BL, et al. High-content single-cell combinatorial indexing. *Nat Biotechnol.* 2021;39:1574-1580. PubMed

## **Developmental Biology**

Schmidt C, Deyett A, Ilmer T, et al. Multi-chamber cardioids unravel human heart development and cardiac defects. *Cell.* 2023;186:5587-5605.e27. <u>PubMed</u>

Zanini F, Che X, Knutsen C, et al. Developmental diversity and unique sensitivity to injury of lung endothelial subtypes during postnatal growth. *Iscience*. 2023;26:106097. PubMed

Zhu H, Wang G, Nguyen-Ngoc K-V, et al. Understanding cell fate acquisition in stem-cell-derived pancreatic islets using single-cell multiome-inferred regulomes. *Dev Cell.* 2023;58:727-743.e11. PubMed

Vuoristo S, Bhagat S, Hydén-Granskog C, et al. DUX4 is a multifunctional factor priming human embryonic genome activation. *Iscience*. 2022;25:104137. <u>PubMed</u>

Casteels T, Bajew S, Reiniš J, et al. SMNDC1 links chromatin remodeling and splicing to regulate pancreatic hormone expression. *Cell Rep.* 2022;40:111288. <u>PubMed</u>

Hofbauer P, Jahnel SM, Papai N, et al. Cardioids reveal self-organizing principles of human cardiogenesis. *Cell.* 2021;184:3299-3317.e22. <u>PubMed</u>

Wang S, Matsumoto K, Lish SR, Cartagena-Rivera AX, Yamada KM. Budding epithelial morphogenesis driven by cell-matrix versus cell-cell adhesion. *Cell*. 2021;184:3702-3716.e30. PubMed

#### Cell Atlas

Ng MTH, Borst R, Gacaferi H, et al. A single cell atlas of frozen shoulder capsule identifies features associated with inflammatory fibrosis resolution. *Nat Commun.* 2024;15:1394. PubMed

Li YE, Preissl S, Miller M, et al. A comparative atlas of single-cell chromatin accessibility in the human brain. *Science*. 2023;382:eadf7044. <u>PubMed</u>

Winter CC, Jacobi A, Su J, et al. A transcriptomic taxonomy of mouse brain-wide spinal projecting neurons. *Nature*. 2023;624:403-414. PubMed

Staupe RP, Lodge KE, Thambi N, et al. Single cell multi-omic reference atlases of non-human primate immune tissues reveals CD102 as a biomarker for long-lived plasma cells. *Commun Biol.* 2022;5:1399. <u>PubMed</u>

Rhodes CT, Thompson JJ, Mitra A, et al. An epigenome atlas of neural progenitors within the embryonic mouse forebrain. *Nat Commun.* 2022;13: 4196. PubMed

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Zhang K, Hocker JD, Miller M, et al. A single-cell atlas of chromatin accessibility in the human genome. *Cell.* 2021;184:5985-6001.e19. <u>PubMed</u>

Li YE, Preissl S, Hou X, et al. An atlas of gene regulatory elements in adult mouse cerebrum. *Nature*. 2021;598:129-136. PubMed

Yao Z, Liu H, Xie F, et al. A transcriptomic and epigenomic cell atlas of the mouse primary motor cortex. *Nature*. 2021;598:103-110. <u>PubMed</u>

## Disease progression

Lareau CA, Dubois SM, Buquicchio FA, et al. Single-cell multiomics of mitochondrial DNA disorders reveals dynamics of purifying selection across human immune cells. *Nat Genet*. 2023;55:1198-1209. <u>PubMed</u>

Schuster SL, Arora S, Wladyka CL, et al. Multi-level functional genomics reveals molecular and cellular oncogenicity of patient-based 3' untranslated region mutations. *Cell Rep.* 2023;42:112840. <u>PubMed</u>

Wang G, Chiou J, Zeng C, et al. Integrating genetics with single-cell multiomic measurements across disease states identifies mechanisms of beta cell dysfunction in type 2 diabetes. *Nat Genet.* 2023;55:984-994. PubMed

Shi Q, Shen Q, Liu Y, et al. Increased glucose metabolism in TAMs fuels O-GlcNAcylation of lysosomal Cathepsin B to promote cancer metastasis and chemoresistance. *Cancer Cell.* 2022;40:1207-1222.e10. PubMed

Murthy PKL, Xi R, Arguijo D, et al. Epigenetic basis of oncogenic-Kras-mediated epithelial-cellular proliferation and plasticity. *Dev Cell.* 2022;57:310-328.e9. <u>PubMed</u>

Husanie H, Abu-Remaileh M, Maroun K, et al. Loss of tumor suppressor WWOX accelerates pancreatic cancer development through promotion of TGF $\beta$ /BMP2 signaling. *Cell Death Dis.* 2022;13:1074. <u>Nature</u>

Kobayashi Y, Masuda T, Fujii A, al. Mitotic checkpoint regulator RAE1 promotes tumor growth in colorectal cancer. *Cancer Sci.* 2021;112:3173-3189. PubMed

Hocker JD, Poirion OB, Zhu F, et al. Cardiac cell type–specific gene regulatory programs and disease risk association. *Sci Adv.* 2021;7:eabf1444. <u>PubMed</u>

#### Neurobiology

Ramakrishnan A, Piehl N, Simonton B, et al. Epigenetic dysregulation in Alzheimer's disease peripheral immunity. *Neuron.* 2024;S096-6273(24)000399-4. <u>PubMed</u>

Pollina EA, Gilliam DT, Landau AT, et al. A NPAS4-NuA4 complex couples synaptic activity to DNA repair. *Nature*. 2023;614:732-741. <u>PubMed</u>

Lu C, Garipler G, Dai C, et al. Essential transcription factors for induced neuron differentiation. *Nat Commun.* 2023;14:8362. <u>Nature</u>

McNamara NB, Munro DAD, Bestard-Cuche N, et al. Microglia regulate central nervous system myelin growth and integrity. *Nature*. 2023;613:120-129. <u>PubMed</u>

Chen R, Liu Y, Djekidel MN, et al. Cell type–specific mechanism of Setd1a heterozygosity in schizophrenia pathogenesis. *Sci Adv.* 2022;8:eabm1077. PubMed

Kaya T, Mattugini N, Liu L, et al. CD8+ T cells induce interferonresponsive oligodendrocytes and microglia in white matter aging. *Nat Neurosci.* 2022;25:1446-1457. <u>PubMed</u>

Zhang Y, Amaral MC, Zhu C, et al. Single-cell epigenome analysis reveals age-associated decay of heterochromatin domains in excitatory neurons in the mouse brain. *Cell Res.* 2022;32:1008-1021. PubMed

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Alkaslasi MR, Piccus ZE, Hareendran S, et al. Single nucleus RNA-sequencing defines unexpected diversity of cholinergic neuron types in the adult mouse spinal cord. *Nat Commun.* 2021;12:2471. PubMed

## **Immunology**

Sun W, Qiu F, Zheng J, et al. CD57-positive CD8+ T cells define the response to anti-programmed cell death protein-1 immunotherapy in patients with advanced non-small cell lung cancer. npj *Precis Onc.* 2024;8:25. <u>Nature</u>

Dufva O, Gandolfi S, Huuhtanen J, et al. Single-cell functional genomics reveals determinants of sensitivity and resistance to natural killer cells in blood cancers. Immunity. 2023;56:2816-2835.e13. <a href="PubMed">PubMed</a>

Khan AUH, Ali AK, Marr B, et al. The TNF $\alpha$ /TNFR2 axis mediates natural killer cell proliferation by promoting aerobic glycolysis. *Cell Mol Immunol.* 2023;20:1140-1155. <u>PubMed</u>

Huuhtanen J, Bhattacharya D, Lönnberg T, et al. Single-cell characterization of leukemic and non-leukemic immune repertoires in CD8+ T-cell large granular lymphocytic leukemia. *Nat Commun.* 2022;13:1981. <u>PubMed</u>

DePasquale EAK, Ssozi D, Ainciburu M, et al. Single-cell multiomics reveals clonal T-cell expansions and exhaustion in blastic plasmacytoid dendritic cell neoplasm. *Front Immunol.* 2022;13:809414. PubMed

Papalexi E, Mimitou EP, Butler AW, et al. Characterizing the molecular regulation of inhibitory immune checkpoints with multimodal single-cell screens. *Nat Genet*. 2021;53:322-331. PubMed



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Chen EC, Gilchuk P, Zost SJ, et al. Convergent antibody responses to the SARS-CoV-2 spike protein in convalescent and vaccinated individuals. *Cell Rep.* 2021;36:109604. PubMed

## Methods development

Carlson RJ, Leiken MD, Guna A, Hacohen N, Blainey PC. A genome-wide optical pooled screen reveals regulators of cellular antiviral responses. *Proc Nat Acad Sci U S A.* 2023;120:e2210623120. <u>PubMed</u>

Chornyi S, Koster J, Waterham HR. Applying CRISPR-Cas9 genome editing to study genes involved in peroxisome biogenesis or peroxisomal functions. *Methods Mol Biol.* 2023;2643:233-245. <u>PubMed</u>

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Peng Q, Huang Z, Sun K, et al. Engineering inducible biomolecular assemblies for genome imaging and manipulation in living cells. *Nat Commun.* 2022;13: 7933. PubMed

Van MV, Fujimori T, Bintu L. Nanobody-mediated control of gene expression and epigenetic memory. *Nat Commun.* 2021;12:537. PubMed

Shareef SJ, Bevill SM, Raman AT, et al. Extended-representation bisulfite sequencing of gene regulatory elements in multiplexed samples and single cells. *Nat Biotechnol.* 2021;39:1086-1094. PubMed